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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,820	09/16/2003	Yukihiro Koike	1089.0410001/TUM	1102

26111 7590 09/29/2005

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 09/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/662,820	KOIKE ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,11 and 16-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11 and 16-19* is/are rejected.

7)☒ Claim(s) *10 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 5/7/04 + 7/27/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SAD

CLAIMS 10, 11 AND 16-19 ARE PRESENTED FOR EXAMINATION

Applicants' amendment, the declaration under 37 C.F.R. § 1.32 of Yukihiro Koike, et al., ("the Koike et al. declaration), and the Information Disclosure Statement filed July 27, 2005 have been received and entered into the application.

Accordingly, claims 1-9 and 12-15 have been canceled; claims 10 and 11 have been amended; and claims 16-19 have been added. Also, as reflected by the attached, completed copy of form PTO/SB/08B, the cited reference has been considered. Also, a copy of the IDS filed May 7, 2004 is attached to the present Office action. As per Applicants' request, reference "AF2" has been lined through due to the erroneous date thereof.

In view of the Koike et al. declaration, the Koike et al. reference relied upon in the previous Office action (i.e., reference "AF2" in the IDS dated May 7, 2004 and reference "AJ2" in the First Supplemental IDS filed July 27, 2005) is no longer relied upon because it has been effectively disqualified as prior art.

In view of the above amendments, all objections/rejections set forth in the previous Office action dated January 27, 2005, except for the following, are withdrawn.

Claim Objection

Claim 10 objected to because of the following informalities:

The claim appears incomplete in that it fails to set forth with what the portal vein is invaded. For the sake of completeness and clarity, i.e., the vein could be invaded by anything, Applicants should amend claim 10 by inserting ---of hepatic cancer cells--- following the

expression "portal venous invasion". Support for this concept may be found in the present specification at page 16, lines 6-19.

Claim 11 is also objected to because the expression "*after treatment* of the hepatocellular carcinoma has occurred"(emphasis added) does not appear to have antecedent basis.

Appropriate correction is required.

Claim Rejection - 35 USC § 102

Legal Standard for Anticipation/Inherency Under - 35 USC § 102

To anticipate a claim under 35 U.S.C. § 102, a single prior art reference must place the invention in the public's possession by disclosing each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to practice the invention. *Scripps Clinic & Research Foundation v. Genetech, Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1001 (Fed. Cir. 1991); *In re Donahue,* 766 F2d531, 533, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985). To anticipate, the prior art must either expressly or inherently disclose every limitation of the claimed invention. *MEHL/Biophile Int'l Corp. v. Milgraum,* 192 F.3d 1362, 1365, 52 U.S.P.Q.2d 1303, 1303 (Fed. Cir. 1999) (citing to *In re Schreiber,* 128 F.3d 1473, 1477, 44 U.S.P.Q. 1429, 1431 (Fed. Cir. 1997)); *Atlas Powder Co. v. Ireco Inc.,* 190 F.3d 1342, 1347, 51 U.S.P.Q.2d 1943, 1946 (Fed. Cir. 1999). To inherently anticipate, the prior art must necessarily function in accordance with, or include, the claimed limitations. *MEHL/Biophile,* 192 F.3d at 1365, 52 U.S.P.Q.2d at 1303. However, it is not required that those of ordinary skill in the art recognize the inherent characteristics or the function of the prior art. *Id.* Specifically, discovery of the mechanism underlying a known process does not make it patentable.

Claims 10 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by

Furukawa et al. (cited by Applicants, cit. ref. "AB2") and STN Registry file Monograph of RN 863-61-6 ("STN Monograph", secondary reference cited only to explain meaning of a term in the primary reference; see MPEP 2131.01(B)), each reference being already of record.

Furukawa et al. teach that the administration of menaquinone-4 (a.k.a. menatetrenone; see STN Monograph at lines 4 and 6 following the heading "OTHER NAMES") to patients suffering from hepatocellular carcinoma was effective to decrease the patients' plasma, i.e., blood, level, of des-gamma-carboxy prothrombin. Menaquinone-4 was administered in dosages of 50 mg. and 10 mg. (dosages encompassed by present claims 17 and 18) are also taught. See the abstract at page 31 and the entirety of page 32.

While Furukawa et al. fail to teach that portal vein invasion was inhibited, in both the present claims and the reference the same active agent was administered to the same patients, i.e., "a patient in need thereof" of present claim 11 equates to the patients suffering from hepatocellular cancer in the reference, it must therefore be that the presently claimed inhibition of portal vein invasion was inherently accomplished by the method of the reference, whether expressly disclosed or not.

Claim Rejection - 35 USC § 103

Claims 10, 11 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furukawa et al. and the STN Registry file Monograph of RN 863-61-6 in view of applicants' acknowledgment in the specification at page 7, lines 1-5 and Wang et al. (cited by applicants cit. ref. "AD2"), each of record, for the reasons of record as set forth in the previous Office action dated January 27, 2005, as applied to claims 1-9 and 11-15, in further view of Koike et al.

(already of record, the Cancer, 2001; 91:561-9 reference, published 2/1/2001 and identified as "AC2" in the IDS filed May 7, 2004).

Claim 10 is properly included because Koike et al. teach that portal vein invasion (of hepatic cancer cells) is developed because of the existence of hepatocellular carcinoma (HCC), (see the abstract, near the middle, "PVI was defined as protrusion of the [HCC] tumor into the first and/or second branch or into the main trunk of the portal vein."). Therefore, because the treatment of HCC was suggested by the references relied on the in the previous Office action, (see pages 8-9 of the previous Office action, absent the reliance on Koike et al.), it would have been obvious that any possible complications resulting from HCC, such as PVI, could also be effectively inhibited. That is, if the causative condition is effectively treated, then it would have been reasonably expected that any condition that occurs because of such condition would also be effectively inhibited from occurring.

Respecting claim 11, because the references suggest an effective treatment in patients for HCC with a vitamin K compound, such would have reasonably suggested the treatment of the HCC in any patient suffering from HCC, including in a patient who had a previous occurrence of HCC. It is believed that such would have been suggested because there would only be two types of patients suffering from HCC, one type that is suffering HCC for the very first time and a second type who had HCC in the past and is again suffering from HCC. Given such a small genus of patient that would have been presented to one of ordinary skill, the treatment of the latter would have been clearly obvious.

Respecting the dosage requirements of new claims 17-19, it has been held that "Generally, differences in concentration or temperature will not support the patentability of

subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" (see MPEP 2144.05(II)). The determination of the optimum dosage regimen to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art and such determination would have been made in accordance with a variety of factors. These would have included the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered a part of a drug combination. Thus, the dosage regimen that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific dosage amounts are not seen to be inconsistent the dosages that would have been determined by the skilled artisan.

Applicant's Arguments

Applicants' remarks at pages 9-12 of their amendment, as they are applicable to the above rejection, have been carefully considered, but fail to persuade the Examiner of error in his determination of obviousness.

In particular, the gist of Applicant's position as to why the rejection(s) are not proper is that "Furukawa [or Wang] does not teach or even suggest the administration of vitamin K-II

(menatetrenone) after a patient has received hepatocellular carcinoma treatment", (see the bottom of Applicants' amendment at page 10 and the sentence bridging pages 11-12).

In response, the Examiner reiterates his position taken above respecting the small size of the genus that would have been possibly treated in the prior art. In particular, because the references suggest an effective treatment in patients for HCC with a vitamin K compound, such would have reasonably suggested the treatment of the HCC in any patient suffering from HCC, including in a patient who had a previous occurrence of HCC. It is believed that such would have been suggested because there would only be two types of patients suffering from HCC, one type that is suffering HCC for the very first time and a second type who had HCC in the past and is again suffering from HCC. Given such a small genus of patient that would have been presented to one of ordinary skill, the treatment of the latter would have been clearly obvious.

Accordingly, the claims are deemed properly rejected.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

September 26, 2005